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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/068,426	02/06/2002	Gray D. Shaw	22058-503	9579

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Ivor R. Elrifi
MINTZ, LEVIN, COHN, FERRIS
GLOVSKY and POPEO, P.C.
One Financial Center
Boston, MA 02111

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/068,426	SHAW ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-9,11-14,20-22,27 and 54-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-9,11-14,20-22,27 and 54-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 1/22/03 .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 4/30/03, is acknowledged.

2. Claims 1, 3, 5-9, 11-14, 20-22, 27 and 54-62 are pending.

Claims 1, 3, 5-9, 11-14, 20-22, 27 and 54-62 are under consideration in the instant application as they read on a fusion polypeptide comprising SEQ ID NO: 1 or SEQ ID NO: 5.

3. In view of the amendment filed on 4/30/03, only the following rejections remained.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1, 3, 5-9, 11-14, 20-22, 27 and 54-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the fusion polypeptide comprising SEQ ID NO:1 or SEQ ID NO:5 for inhibiting platelet aggregation; does not reasonably provide enablement for any polypeptide comprising a first polypeptide operably linked to a second polypeptide, wherein the first polypeptide **comprises** any polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Ibα polypeptide of SEQ ID NO:1 and said first polypeptide binds a polypeptide selected from the group consisting of leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin; and wherein the second polypeptide **comprises** at least any region of an immunoglobulin heavy chain polypeptide in claim 1; wherein said first polypeptide binds to at least two of the polypeptides selected from the group consisting of leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin in claim 3, wherein said fusion polypeptide is more resistant to proteolysis than a wild-type GP Ibα polypeptide in claim 6, wherein said first polypeptide binds with higher affinity to a von Willebrand factor polypeptide than a wild type glycoprotein Ibα polypeptide binds to said von Willebrand factor polypeptide in claim 7, wherein said first polypeptide comprises at least one of the amino acid substitutions G233V or M239V relative to the amino acid sequence of a wild-type GPIbα polypeptide in claim 8, wherein said first polypeptide comprises the amino acid substitutions G233V or M239V relative to the amino acid sequence of a wild-type GPIbα polypeptide in claim 9, wherein said second polypeptide comprises an Fc-region of an immunoglobulin heavy chain in claim 11; any multimeric polypeptide comprising the fusion polypeptide of claim 1 in claim 21, wherein said multimeric polypeptide is a dimmer in claim 22, a pharmaceutical composition comprising the fusion polypeptide of claim 1 in claim 27, wherein said first polypeptide binds at least three polypeptides selected from the group consisting of leukocytes integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin in claim 54, wherein said first polypeptide binds leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin in claim 55, wherein said first polypeptide binds leukocyte integrin Mac-1 polypeptide in claim 56,

wherein said first polypeptide binds von Willebrand factor in claim 57, wherein said first polypeptide binds thrombin in claim 58, wherein said first polypeptid4e binds P-selection in claim 59; any fusion polypeptide comprising a fist polypeptide operably linked to a second polypeptide wherein the first polypeptide consists essentially of a polypeptide sequence with at least 85% homology to an extracellular portion of a glycoprotein Ibα polypeptide of SEQ ID NO:1 and said first polypeptide binds von Willebrand factor polypeptide and wherein said second polypeptide consists essentially of an immunoglobulin heavy chain polypeptide, wherein said immunoglobulin heavy chain polypeptide comprises a Fc region in claim 60. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action mailed 01/30/03.

6. Claims 1, 3, 5-9, 11-14, 20-22, 27 and 54-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action mailed 01/30/03.

Applicant's arguments, filed 04/30/03, have been fully considered, but have not been found convincing.

Applicant argues that methods for making polypeptides falling within the scope of the claims are known in the art and are additionally discussed at page 7 and 12-30 of the specification. Applicant further argues that methods for detecting binding of a Gp Ibα protein to a ligand such as those recited in claim 1 are also well known in the art (e.g., Simon et al). Applicant concluded that one of ordinary skill in the art can readily practice the full scope of the invention now claimed. Applicant further asserts that the specification makes clear that Applicants were in full possession of the invention now claimed when they filed the application, wherein the specification discloses six examples of polypeptides falling within the scope of the claims.

Applicant is relying upon certain biological activities and the disclosure of six species to support an entire genus. The claims as written encompass a broad genus of polypeptides with an unlimited number of possibilities with regard to the length of the polypeptide sequence. Further, the enablement issues of making the protein still remain because the specification does not teach and provide sufficient guidance as to which amino acid of SEQ ID NO:1 would have been altered such that the resultant polypeptide would have retained the function of inhibiting platelet aggregation. In addition, variation up to 15% of SEQ ID NO: 1 (81×19^{15}) provide a range of activities, not all which are necessarily predictive of binding to leukocyte integrin Mac-1 polypeptide, von Willebrand factor, thrombin and P-selectin. Therefore, absent the ability to predict which of these polypeptides would function as claimed, and given the lack of data on regions critical for activity, for one of skill in the art to practice the invention as claimed would require a level of experimentation that is excessive and undue.

It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence and the functional properties of the different parts of the protein. The specification does not teach which changes in the amino acid of SEQ ID NO:1 would not alter all the activities of the polypeptides. Therefore, the specification fails to provide sufficient guidance as to which core structure of SEQ ID NO: 1 is essential for maintain its biological activity and which changes can be made in the structure of SEQ ID NO: 1 and still maintained the same function.

Regarding applicant's argument that that the specification provides a working example and substantial guidance on how to identify polypeptides that have the recited activity, the examiner notes that in order to satisfy the prong of U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to screen to identify the invention. Until the time when the at least 85% sequence identity polypeptides are found, then one skill in the art can make them. The skilled artisan would have been able to prepare the claimed protein.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 3, 11-14, 20-22, 27 and 54-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over in Lopez JA et al (Proc Natl Acad Sci U S A. 84:5615-5619, 1987) view of U.S. Patent No. 6,277,975 for the same reasons set forth in the previous Office Action mailed 01/30/03.

Applicant's arguments, filed 04/30/03, have been fully considered, but have not been found convincing.

Applicant asserts that the examiner has the initial burden of establishing that the teachings of the applied art would have suggested the claimed invention to one of ordinary skill in the art and that such person would have had reasonable expectation of success. Applicant further asserts that the suggestion must be in the prior art and not in the Applicants' disclosure. Applicant argues that the Examiner has improperly relied on Applicants' specification to find motivation for

combining the references. Applicant asserts that the specification teaches the claimed glycoprotein-Ibα-derived fusion proteins are useful for treating vascular conditions associated with vascular inflammation, including thrombosis, atherosclerosis, and angioplasty-related restenosis, The second polypeptide of the fusion protein can enhance the half-life of the fusion protein. Applicant concluded that a motivation for making the claimed invention is to enhance the anti-inflammatory effects of the glycoprotein-Ibα by adding the second polypeptide. Applicant argues that Lopez provides a general review of the properties of glycoprotein Iba and describes the closing of a human glycoprotein Ibα cDNA. However, Lopez et al say nothing about its therapeutic usefulness in treating vascular associated inflammation. Applicant argues that the '975 patent fails to overcome the deficiencies of Lopez et al. The '975 patent is completely silent about glycoprotein Ibα, or about therapeutic uses of a fusion protein that includes all or part of the glycoprotein. Applicant further argues that there is no teaching in the applied references as to why one of ordinary skill in the art would combine them to arrive at the claimed invention. Applicant contends that the Examiner has engaged in impermissible hindsight to arrive at the conclusion that the claimed invention is obvious over Lopez in view of the '975 patent.

In response to Applicant's argument that the Examiner's has improperly relied on Applicant's specification to find motivation for combining the references, it is clear that the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin, 170 USPQ 209 (CCPA 1971).

In response to applicant's arguments against the references individually, one cannot show non - obviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

The claimed functional limitation would be expected properties. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable.

9. Claims 1, 3, 5-9, 10-14, 20-22, 27 and 54-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over in Miura *et al* (J Biol Chem. 275:7539-7546) in view of U.S. Patent No. 6,277,975 for the same reasons set forth in the previous Office Action mailed 01/30/03.

Applicant's arguments, filed 04/30/03, have been fully considered, but have not been found convincing.

Applicant argues that Miura et al teach that the calmodulin was used in the fusion protein because it bound to the pheothiazine derivative W-7 agarose. Applicant further argues that there is no teaching in Miura that a GPIbα-derived fusion protein is useful for treating vascular-associated inflammation, nor is there any suggestion in this reference for making a GPIbα-derived fusion protein for any purpose other than to facilitate subsequent purification for in vitro biochemical binding studies. Applicant concluded that the combination of Miura and the '975 patent and produces the claimed invention only through impermissible hind-sight reconstruction.

Contrary to applicant's assertion Miura et al teaches that the Von Willebrand factor (VWF)1 is a multimeric plasma glycoprotein that plays a crucial role in primary hemostasis by enabling platelets to adhere at sites of vascular injury. Platelet adhesion requires the binding of VWF to the platelet membrane glycoprotein (GP) Ib-IX complex (see introduction in particular).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. In re McLaughlin, 170 USPQ 209 (CCPA 1971).

The claimed functional limitation would be expected properties. Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable.

10. Claims 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miura *et al* (J Biol Chem. 275:7539-7546) view of U.S. Patent No. 6,277,975 as applied to claim 1, 3, 5-9, 10-14, 20-22, 27 and 54-60 above, and further in view of U.S Patent No. 5,340,727 for the same reasons set forth in the previous Office Action mailed 01/30/03.

Applicant's arguments, filed 04/30/03, have been fully considered, but have not been found convincing.

Applicant contends that the Examiner points to no motivation or suggestion in this reference for producing the invention.

Contrary to the applicant assertion the '727 patent teaches a motivation to insert the signal peptide because the signal peptide causes the polypeptide to be recognized by cellular structures as a polypeptide of the kind to be processed for ultimate secretion from the cell, with concomitant cleavage of the signal polypeptide from the mature GPIbα polypeptide.

11. The following new ground of rejection is necessitated by the amendment filed on 4/30/03.

12. Claims 3, 54 and 62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

The phrase "binds to at least two of the polypeptides" claimed in claim 3, line 2, "binds to at least three of the polypeptides" claimed in claim 54, line 2 and "consists essentially of" claimed in claim 62 line 2 represent a departure from the specification and the claims as originally filed.

Applicant's amendment filed 4/30/03 points to the specification and claims for support for the newly added limitations "binds to at least two of the polypeptides", "binds to at least three of the polypeptides" and "consists essentially of" as claimed in claims 3, 54 and 62, respectively. However, the specification does not provide a clear support for such limitation. The instant claims now recite limitations which were not clearly disclosed in the specification and recited in the claims as originally filed.3

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
October 28, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600